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Risk Factors for Asthma up to 16 Years of Age*

Evidence from a National Cohort Study

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From a national cohort of 8,806 children examined at ages seven, 11 and 16 years (National Child Development Study), data on asthma or wheezing illness (AW) were analyzed to describe its natural history in childhood and its risk factors. Factors found to predict the subsequent onset of asthma included male sex of child, mother's age at the child's birth, pneumonia, whooping cough, tonsillectomy/adenoidectomy, allergic rhinitis, eczema and periodic abdominal pain/vomiting attacks. A wide range of perinatal factors, including feeding practices, and social and family factors were shown to have no effect on natural history.

Much of the existing epidemiologic evidence about the etiology of asthma rests on prevalence and follow-up studies and there is a serious lack of population-based cohort data. The National Child Development Study (NCDS)[1] originated in the National Perinatal Study[2] and went on to become a multipurpose cohort study of child development including health. While it was not designed specifically to study the epidemiology of asthma, it is nevertheless possible to obtain valuable information relating to the natural history of asthma. This article describes some of the findings from our analysis of NCDS data which have implications for the etiology of asthma.

Materials and Methods

The NCDS followed-up at ages seven, 11 and 16 all children in England, Scotland and Wales born during one week of March, 1958. At each follow-up, information about current or past asthma or wheezing illness was obtained as part of a structured questionnaire on medical and other topics administered to parents by health visitors. The wording of the asthma questions varied at each interview but it was nevertheless possible to classify subjects at each interview into three categories: no asthma or wheezing, previous asthma or wheezing but not in the past 12 months, and current asthma or wheezing (symptoms reported in the past 12 months). Based on these three possibilities at each of three interviews, 27 mutually exclusive natural history categories can be created. Some of these contain small numbers or are of limited clinical or epidemiologic interest, and so for the purpose of the present analysis a collapsed classification of six natural history categories was used.

These natural history categories were analyzed in relation to medical and social data collected at each of the follow-up medical examinations and home interviews. Factors that have previously been reported to be associated with asthma or wheezing were selected together with those considered likely to influence the natural history of asthma.

The overall association between a variable and the natural history category was tested using the Chi-squared test or one-way analysis of variance as appropriate. Where there was a statistically significant overall association, the relative risks of each natural history category were calculated. The statistical significance of the relative risk was tested by calculating 95 percent confidence intervals.

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Table 1—*Lifetime Incidence of Asthma or Wheezing (n = 8,806)*

Age at interview (yrs)	Asthma or wheezing at any time in past (percent)	
	Cross-sectional	Cumulative*
7	18.3	18.3
11	12.1	21.9
16	11.6	24.7

*Using information from previous interviews

Table 2—*Prevalence of Asthma or Wheezing in 12 Months Preceding Interview (n = 8,806)*

Age at interview (yrs)	Asthma or Wheezing in past 12 months (percent)	
	Cross-sectional	Cumulative*
7	8.3	8.3
11	4.7	10.7
16	3.5	11.1

*Using information from previous interviews

Results

Data on asthma or wheezing were obtained at all three ages for 8,806 of the original NCDS cohort of over 15,000 children living in England, Scotland and Wales and available for follow-up at seven years.

The reported lifetime incidence of asthma or wheezing is shown in Table 1. Using data from all three interviews, a total of 24.7 percent of children had experienced asthma or wheeze by the age of 16 years. When questioned at age 16 years, however, the proportion reporting past asthma or wheeze was less than half this figure (11.6 percent). The prev-

Table 3—*Prognosis of Asthma or Wheezing if Current (past 12 months) at Age 7 (n = 731)*

Persistence of AW and age (yrs)	Percent of 7 year-olds who reported current AW
Current at 11	28.3
Current at 16	16.3
Current at 11 *and* 16	10.5
Current at 11 *or* 16	34.1
Not current at 11 or 16	65.9

Table 4—*Natural History Categories (n = 8,806)*

Category	Percent of sample
Never had asthma or wheezing	75.3
Onset before age 7 but not current at 7 or reported subsequently	8.6
Current at age 7 but not reported subsequently	5.5
Onset age 0 to 7 and also reported at 11 or 16	4.2
Onset age 8 to 11	3.6
Onset age 12 to 16	2.8

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Table 5—*Factors Predicting the Onset of Asthma or Wheezing*

Predictive factors	Overall χ^2 P value	Relative risk of:	Natural history: By age 7 not after	At age 7 not after	Age 0-7 and after	Age 8-11 onset	Age 12-16 onset
Perinatal							
Sex of child	<0.001	Boy: girl	1.1	1.2	1.4*	1.3*	1.4*
Mother's age	<0.001	15-19: 20-29 yrs	1.4*	1.5*	1.1	1.9*	1.7*
		15-19: 30+ yrs	1.6*	1.3	1.3	1.9*	2.0*
		20-29: 30+ yrs	1.2	0.9	1.1	1.0	1.2
Smoking in pregnancy	<0.001	Smoker: Non-smoker	1.3*	1.2	0.8	1.0	1.0
Region of child's birth	<0.01	North: Centre	0.7*	0.9	0.9	0.7	1.0
		North: South	0.8*	0.9	1.0	0.9	1.0
		Centre: South	1.1	1.0	1.0	1.2	1.0
Assessed at 7							
History of pneumonia	<0.001	Yes: No	2.0*	2.0*	4.3*	1.5	1.8*
Tonsillectomy/ adenoidectomy	<0.001	Yes: No	1.3*	1.2	1.2	1.2	1.4*
Eczema in 1st year	<0.001	Yes: No	1.2	1.4	5.4*	1.7*	1.5
Eczema after 1st year	<0.001	Yes: No	1.1	1.3	4.7*	1.3	1.7*
Eczema on Dr. exam.	<0.001	Yes: No	0.8	1.1	4.9*	1.6	2.1*
Hayfever or sneezing ever	<0.001	Yes: No	1.3	2.0*	7.1*	1.5	1.7*
Periodic vomiting or bilious attacks ever	<0.001	Yes: No	1.2*	1.4*	1.8*	0.8	1.4*
Periodic abdominal pain ever	<0.001	Yes: No	1.4*	1.3*	1.5*	0.9	1.4*
Assessed at 11							
Whooping cough ever	<0.001	Yes: No	1.2*	1.3*	1.4*	1.4*	1.4*
Eczema in past year	<0.001	Yes: No	1.2	1.2	4.2*	1.9*	1.7*
Hayfever or allergic rhinitis in past year	<0.001	Yes: No	1.0	1.2	5.2	2.2*	1.9*

*P<0.05

alence of current asthma was highest at seven years (8.3 percent) but had fallen to 3.5 percent at 16 years (Table 2). At each interview, the lifetime and current rates for the present cohort (those with data available at all interviews) were similar to those among subjects interviewed only once or twice. Of those with current symptoms at seven, 28 percent reported current symptoms at 11 years, 16 percent at 16 years and 11 percent at both ages (Table 3).

For the purpose of analysis, the 27 patterns of questionnaire response were collapsed into the six categories described in Table 4.

From an etiologic standpoint two types of relationship could be discerned. In the first, a given factor was assessed prior to the onset of asthma or wheeze, and could therefore be considered predictive. In the other, the order of occurrence of the factor and the onset of asthma or wheezing could not, from the data available, be shown to be predictive because the assessment of both factors was concurrent. Most factors found to be predictive are shown in Table 5 together with their relative risks. Any concurrent associations for these variables are also shown. Of the perinatal factors the most prominent was sex of the child and the mother's age at birth of the child. Multifactorial analysis was done to explore whether social class or breast feeding might explain this latter relationship, but this was not the case.

Of the factors assessed at seven or 11 years, the main ones predicting subsequent onset of asthma or wheezing were atopic conditions—eczema or allergic rhinitis—and (at seven years only) periodic vomiting or abdominal pain. A history of pneumonia (at seven years) and whooping cough (at 11 years) were also predictive. Previous tonsillectomy or adenoidectomy reported at age seven years predicted onset in adolescence (though not when reported at 11 years).

Those factors which were concurrently associated with asthma or wheezing but not predictive are shown in Table 6. They mainly comprise upper and lower respiratory conditions but also include fits or convulsions in the first year (but not continuing into later life), enuresis, headaches and one adverse socioeconomic factor—sharing of one or more household facilities.

Those factors not associated with natural history are listed in Table 7. Notably, these included breast feeding, social class and a variety of indicators of socioeconomic circumstances and family stress.

Assessment of smoking in the household was inadequate, available only for the mother while she was pregnant and for both parents when the child was 16 years old. Smoking in pregnancy was associated only with an increased relative risk of asthma or wheezing during the early years of life and smoking by one or both parents reported when the child was 16 years was not related. At 16 years, the child's own smoking habit was unrelated to the presence of asthma or wheezing.

Discussion

The National Child Development Study was not designed to examine the etiology of asthma and there are a number of

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unassociated with natural history anyway). Further analysis found that the effect of maternal age existed within the 16 to 19-year-old age group as well. This finding needs to be confirmed by other studies and we can offer no plausible theory to explain it.

The increased risk of asthma or wheezing in boys agrees with other studies,[9] though our results differ from most in that the effect of male sex did not diminish as the age of onset of asthma increased.

The question of whether breast feeding protects against childhood asthma is of great importance since, if true, it would offer insights into etiology and a method of prevention. The evidence is patchy, but a prospective study by Blair[9] found that asthma was more likely to persist in those who were bottle fed. Our results do not confirm this finding, nor was any other effect of infant feeding practice on natural history apparent.

The association between natural history of asthma or wheezing and other atopic conditions confirms the abundant evidence from other prevalence and case-control studies. Additionally, however, we have demonstrated that periodic abdominal pain or vomiting attacks are also predictive and that headaches or migraine are an important concurrent association, though falling just short of significance as a predictive factor. Such associations have also been observed in a separate prevalence study[4] and can no longer be regarded as speculative. We feel that elucidation of the nature of these associations is an important research priority.

The last group of factors found to predict the onset of asthma or wheezing in adolescence were chest infections (pneumonia and whooping cough) and this finding has an important bearing on the question of whether and how early childhood chest troubles may predispose to chronic lung disease in later life as indicated in a previous prospective[10] and retrospective study.[11]

There are various explanations for the associations we have observed. The report of pneumonia or whooping cough may have been a mistaken diagnosis for what was in reality asthma. Chest infection may have led to the later onset of asthma by creating some predisposition which remained latent until adolescence. Both chest infections and asthma may have a common environmental cause or may be the result of a common predisposition via some kind of general "chesty" tendency. Perhaps the asthmatic tendency itself could predispose to chest infections and in some circumstances the chest infection might be expressed prior to the first attack of asthma.

Data about wheezing symptoms and chronic productive cough have been collected from this same cohort at the age of 23 years. Analysis of this additional information should provide further important evidence concerning the origins of both asthma and chronic bronchitis.

Conclusions

The National Child Development Study is an important source of nationally representative longitudinal data. While not specifically designed to study asthma, analysis of the data has elucidated a number of factors that predict the subsequent onset of asthma. These include male sex of the child, mother's age at child's birth, pneumonia, whooping cough, tonsillectomy/adenoidectomy, allergic rhinitis, eczema and periodic abdominal pain/vomitting attacks.

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Occupational Asthma

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This article reviews recent developments in the study of occupational asthma and implications for the overall understanding of asthma. Occupational asthma is a clinical syndrome caused by many different agents. Contribution of studies of experimental inhalation challenge using occupational agents to the knowledge of asthmatic reactions and their mechanisms is discussed. Investigations in the occupational environment into predisposing factors and persistence or recovery after exposure to an allergic agent or nonspecific irritant are reviewed. Approaches to diagnosing asthma in the occupational environment and to assessing functional impairment and disability are outlined. Directions for future research are identified.

Studies in occupational asthma have provided considerable insight into the various etiologic factors, possible pathogenetic mechanism and, to a certain extent, the clinical course of asthma. For the purpose of this presentation, occupational asthma will be defined as asthma caused by a

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